IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:
Shigeo TAKADA et al.
Serial No. 10/030,170 Group Art Unit: 1614
Filed: April 22, 2002 Examiner: Weddington, Kevine
(I.A.filed August 9, 2000)
For: THERAPEUTIC AGENT FOR DIABETES

DECLARATION UNDER 37 CFR 1.132

Honorable Commissioner of Patents and Trademarks,
Washington, D.C. 20231

Sir:

I, Shigeo TAKADA, (citizenship; Japan, residence; 517-2, Higashitomioka, Isehara-shi, kanagawa, Japan, 259-1112) declare and say that:

I withdrew from Graduate School of Tokushima University on March 1973.

I received Doctor of Health Science on September 1980.

I am conducting research at Medical School of Tokai University

I am a co-inventor of the subject matter of the above-identified application.

I declare further that the following experiments were conducted at my direction and under my supervision and the results are true and correct to the best of my knowledge.

Experiments

(1) Purpose of Experiment

db/db mouse is a model mouse which shows adiposis due to edacity and then develops type II diabetes. The purpose of experiment is to study whether the transition from moderately high blood sugar state to type II diabetes can be prevented by administering a mixture of poly lactic acids to db/db mouse which shows moderately

high blood sugar level.

(2) Methods

6 week db/db mice (female) were purchased from CLEA Japan Inc. Standard solid food (CE2) and water were given to the mice ad lib for 17 days. At 18th day, administration of a mixture of poly lactic acids was started. The administration amount is 0.4mg/50g body weight/day. The mixture of poly lactic acids was suspended in water just before use, and was orally administered by stomach tube. The administration was carried out in the morning every day. Before the administration, and at 7th day and 49th day from the start of the administration, the blood sugar level was quantified. The quantification was carried out by O-toluidine/boric acid method. After measuring the blood sugar level at the 49th day, the mice were euthanized, and the pancreases were extracted. The pancreases were immediately fixed with Bouin and stained with aldehyde/fuchsin

(3) Results

(i) Biological results

	Administration Period		
	0 day	7th day	49th day
Control group	140	155	280
Administration group with a mixture of poly lactic acids	185	110	140

The values in the table show the blood sugar level in mg/dl.

*: 140mg/dl is near upper limit of normal blood sugar level

(ii) Morphological results

In the normal mouse pancreas (photograph-A), the morphology of islet of Langerhans is clear, and many numbers of insulin-secreting granules are observed. In the pancreas of the control group at the 49th day (photograph-B), the morphology of islet of Langerhans is considerably destroyed, and few insulin-secreting granules are observed. The slightly remaining insulin-secreting granules show an inferior stainability, suggesting that the amount of insulin in the granules is small. In the

pancreas of the administration group at the 49th day (photograph-C), a larger number of insulin-secreting granules are observed than the pancreas of the control group. These insulin-secreting granules show an excellent stainability, suggesting that large amount of insulin is contained in the granules.

(4) Conclusion

As shown in the above, by administering a mixture of poly lactic acids to a model mouse with moderately high blood sugar level, the morphology of islet of Langerhans can be maintained, the blood sugar level can be maintained within the normal scope, and the transition from moderately high blood sugar state to type II diabetes can be prevented and thus the progress of the diabetes can be prevented.

I declare further that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application of any patent issuing thereon.

Dated this day of January, 2003.

15, Jan., 2003

Shigeo Takada

Shigeo TAKADA